LETTER TO THE EDITOR

To the Editor:—A series of *JGIM* articles have omitted important information regarding guidelines for anticoagulation therapy for venous thromboembolism.¹⁻⁷ For instance, Ganz et al. said, "Guidelines for oral anticoagulation after deep venous thrombosis (DVT) or pulmonary embolism (PE) have recommended that patients be anticoagulated for at least 3 months after hospital discharge."¹ This implies that randomized controlled trials support this guideline, which they do not.

Your authors and the researchers in the articles that they referenced did not mention or discuss a randomized controlled trial published in the *Journal* by Nielsen et al., comparing heparin and a phenprocoumon anticoagulation with phenylbutazone in patients with DVT.^{8,9} This is the only published randomized controlled trial of treatment of DVT patients with unanticoagulated controls versus standard anticoagulation. It was a negative study with 1/48 anticoagulated patients dying of pulmonary emboli and 0/42 phenylbutazone patients with fatal PE.

Heparin and vitamin K antagonists became standard treatment for DVT and PE patients in the 1940s before the advent of randomized controlled trials to prove efficacy. The FDA allowed them to be "grandfathered in" as standard treatment of DVT and PE in the early 1960s when proof of efficacy became required for FDA approval. Low-molecular-weight heparins (LMWHs) have been granted indications for treatment of DVT and PE by virtue of randomized controlled trials showing equivalence with heparin in comparisons that do not include unanticoagulated controls.

None of the other major reviews of the treatment of venous thromboembolism (VTE) and none of the published trials of LMWH in VTE treatment mention the Nielsen study. Last year, I spoke with Lilia Talarico, MD, Chief of the Coagulation and GI Drug section of the Center for Drug Evaluation and Research (CDER) of the American FDA, who did not know then of the Nielsen study. However, based on this important trial and an

overall review of the data, Janet Woodcock, MD, Chief of CDER, Robert Temple, MD, FDA Director, Office of Medical Policy, and Dr. Talarico are considering the withdrawal of the indication for anticoagulants (heparin, LMWH, and vitamin K antagonists) in prophylaxis and treatment of VTE.

For the articles and FDA correspondence detailing the case for withdrawing the indications for anticoagulants (heparin, LMWHs, and vitamin K antagonists) in prophylaxis and treatment of VTE, please see my website:<http://hometown.aol.com/~dkcundiff/home.htm>. — **DAVID K. CUNDIFF, MD.**

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